

# NMCP COVID-19 Literature Report #65: Friday, 09 April 2021

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**Purpose:** These reports, published every other week on Fridays, are curated collections of current research, evidence reviews, special reports, grey literature, and news regarding the COVID-19 pandemic that may be of interest to medical providers, leadership, and decision makers.

All reports are available online at <https://nmcp.libguides.com/covidreport>. Access is private; you will need to use the direct link or bookmark the URL.

**Disclaimer:** I am not a medical professional. This document is current as of the date noted above. While I make every effort to find and summarize available data, I cannot cover everything in the literature on COVID-19. Please feel free to reach out with questions, suggestions for future topics, or any other feedback.

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## The Big Picture

### *News in Brief*

COVID-19 was the third leading cause of death in 2020, after heart disease and cancer ([NPR](#); see also: MMWR reports linked below in *Peer-Reviewed Articles*).

"Are we entering a 'fourth wave' of the pandemic? Experts disagree" ([WashPo](#)).

The CDC has updated travel guidance for people who are fully vaccinated—basically, no need for self-quarantine and take the usual precautions during travel ([CDC](#)).

The FDA has authorized 2 more rapid at-home tests for COVID-19 ([FDA](#)).

The pandemic may have set back global gender parity by a generation ([WashPo](#); see [WEF's Global Gender Gap Report 2021](#) for details).

"Scientists need to admit what they got wrong about COVID: Over the last year, the scientific community has been reluctant to openly discuss its missteps. But coming clean could help prevent the next pandemic" ([Wired](#)).

### *Virus Origins*

"WHO report into COVID pandemic origins zeroes in on animal markets, not labs: Scientists say the conclusions make sense but note that supporters of the lab-leak theory are unlikely to be satisfied" ([Nature](#); see also: [Twitter thread](#) from article's author; full, 320-page report from WHO linked below in *Special Reports*).

"After the WHO report: what's next in the search for COVID's origins – a World Health Organization report makes a reasonable start, scientists say, but there are many questions yet to be answered" ([Nature](#)).

## *Peer-Reviewed Articles*

JAMA: [Excess Deaths From COVID-19 and Other Causes in the US, March 1, 2020, to January 2, 2021](#) (02 April 2021)

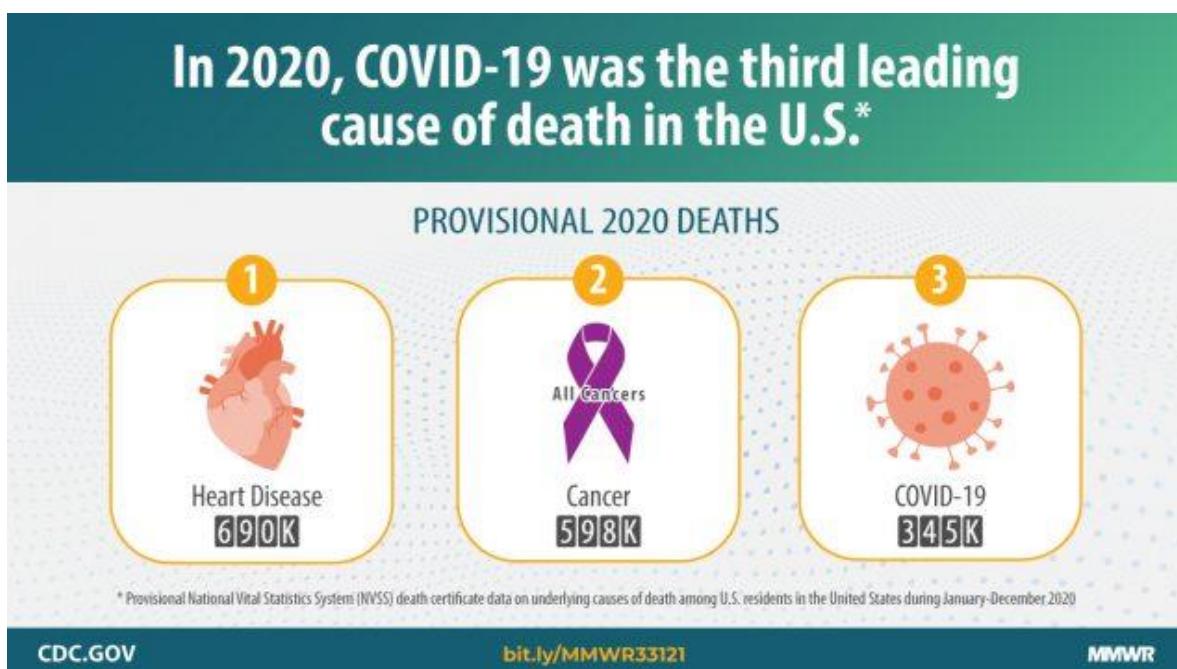
"This study updates an analysis of US mortality in 2020, including deaths due to COVID-19 as well as all other causes."

MMWR: [Provisional Mortality Data — United States, 2020](#) (31 March 2021)

"What is already known about this topic? The COVID-19 pandemic caused approximately 375,000 deaths in the United States during 2020.

What is added by this report? The age-adjusted death rate increased by 15.9% in 2020. Overall death rates were highest among non-Hispanic Black persons and non-Hispanic American Indian or Alaska Native persons. COVID-19 was the third leading cause of death, and the COVID-19 death rate was highest among Hispanics.

What are the implications for public health practice? Provisional death estimates provide an early indication of shifts in mortality trends. Timely and actionable data can guide public health policies and interventions for populations experiencing higher numbers of deaths that are directly or indirectly associated with the COVID-19 pandemic."



MMWR: [Death Certificate–Based ICD-10 Diagnosis Codes for COVID-19 Mortality Surveillance – United States, January–December 2020](#) (31 March 2021)

"What is already known about this topic? During 2020, approximately 375,000 U.S. deaths were attributed to COVID-19.

What is added by this report? Among 378,048 death certificates from 2020 listing COVID-19, 5.5% listed COVID-19 without codes for any other conditions. Among 357,133 death certificates with at least one other condition, 97% had a co-occurring diagnosis of a plausible chain-of-event condition (e.g., pneumonia or respiratory failure), or a significant contributing condition (e.g., hypertension or diabetes), or both.

What are the implications for public health practice? These findings support the accuracy of COVID-19 mortality surveillance in the United States using official death certificates. High-quality documentation of death certificate diagnoses is essential for an authoritative public record."

### ***Special Reports***

GAO: [COVID-19: Sustained Federal Action Is Crucial as Pandemic Enters Its Second Year](#) (31 March 2021)

"In our 6th comprehensive report on the federal response to the pandemic, we identified multiple ways agencies can improve response efforts. For example, we recommended improvements in federal data to provide a clear picture of whether COVID-19 vaccines are being distributed equitably to communities of color, which are disproportionately affected by the virus. We also recommended that federal agencies establish controls to combat potential fraud.

As of January 2021, we had made 44 recommendations to agencies; 6 have been implemented. This report makes 28 new recommendations. Agencies should swiftly take action to address all recommendations."

WHO: [WHO-convened global study of origins of SARS-CoV-2: China Part](#) (30 March 2021)

"In May 2020, the World Health Assembly in resolution WHA73.1 requested the Director-General of the World Health Organization (WHO) to continue to work closely with the World Organisation for Animal Health (OIE), the Food and Agriculture Organization of the United Nations (FAO) and countries, as part of the One Health approach, to identify the zoonotic source of the virus and the route of introduction to the human population, including the possible role of intermediate hosts. The aim is to prevent both reinfection with the virus in animals and humans and the establishment of new zoonotic reservoirs, thereby reducing further risks of the emergence and transmission of zoonotic diseases."

### **SARS-CoV-2 Variants**

#### ***News in Brief***

The UK variant (B.1.1.7) is now the dominant strain in US, according to the CDC ([NPR](#)).

The E484K mutation (nicknamed "Eek") in Tokyo may reduce vaccine protection ([Reuters](#)).

"Rise of coronavirus variants will define the next phase of the pandemic in the U.S." ([WashPo](#)).

### ***Peer-Reviewed Articles***

Lancet: [Efficacy of ChAdOx1 nCoV-19 \(AZD1222\) vaccine against SARS-CoV-2 variant of concern 202012/01 \(B.1.1.7\): an exploratory analysis of a randomised controlled trial](#) (30 March 2021)

The AstraZeneca vaccine and the UK variant:

"Volunteers (aged  $\geq 18$  years) who were enrolled in phase 2/3 vaccine efficacy studies in the UK, and who were randomly assigned (1:1) to receive ChAdOx1 nCoV-19 or a meningococcal conjugate control (MenACWY) vaccine, provided upper airway swabs on a weekly basis and also if they developed symptoms of COVID-19 disease (a cough, a fever of  $37.8^{\circ}\text{C}$  or higher, shortness of breath, anosmia, or ageusia). Swabs were tested by nucleic acid amplification test (NAAT) for SARS-CoV-2 and positive samples were sequenced through the COVID-19 Genomics UK consortium. Neutralising antibody responses were measured using a live-virus microneutralisation assay against the B.1.1.7 lineage and a canonical non-B.1.1.7 lineage (Victoria). The efficacy analysis included symptomatic COVID-19 in seronegative participants with a NAAT positive swab more than 14 days after a second dose of vaccine. Participants were analysed according to vaccine received. Vaccine efficacy was calculated as 1 – relative risk (ChAdOx1 nCoV-19 vs MenACWY groups) derived from a robust Poisson regression model. This study is continuing and is registered with ClinicalTrials.gov, NCT04400838, and ISRCTN, 15281137.

Participants in efficacy cohorts were recruited between May 31 and Nov 13, 2020, and received booster doses between Aug 3 and Dec 30, 2020. Of 8534 participants in the primary efficacy cohort, 6636 (78%) were aged 18–55 years and 5065 (59%) were female. Between Oct 1, 2020, and Jan 14, 2021, 520 participants developed SARS-CoV-2 infection. 1466 NAAT positive nose and throat swabs were collected from these participants during the trial. Of these, 401 swabs from 311 participants were successfully sequenced. Laboratory virus neutralisation activity by vaccine-induced antibodies was lower against the B.1.1.7 variant than against the Victoria lineage (geometric mean ratio 8·9, 95% CI 7·2–11·0). Clinical vaccine efficacy against symptomatic NAAT positive infection was 70·4% (95% CI 43·6–84·5) for B.1.1.7 and 81·5% (67·9–89·4) for non-B.1.1.7 lineages.

ChAdOx1 nCoV-19 showed reduced neutralisation activity against the B.1.1.7 variant compared with a non-B.1.1.7 variant in vitro, but the vaccine showed efficacy against the B.1.1.7 variant of SARS-CoV-2."

Clin Infect Dis: [Phylogenetic analyses of SARS-CoV-2 B.1.1.7 lineage suggest a single origin followed by multiple exportation events versus convergent evolution](#) (27 March 2021)

"The emergence of new variants of SARS-CoV-2 herald a new phase of the pandemic. This study used state-of-the-art phylodynamic methods to ascertain that the rapid rise of B.1.1.7 "Variant of Concern" most likely occurred by global dispersal rather than convergent evolution from multiple sources."

Nat Med: [Sensitivity of infectious SARS-CoV-2 B.1.1.7 and B.1.351 variants to neutralizing antibodies](#) (26 March 2021)

"Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) B.1.1.7 and B.1.351 variants were first identified in the United Kingdom and South Africa, respectively, and have

since spread to many countries. These variants harboring diverse mutations in the gene encoding the spike protein raise important concerns about their immune evasion potential. Here, we isolated infectious B.1.1.7 and B.1.351 strains from acutely infected individuals. We examined sensitivity of the two variants to SARS-CoV-2 antibodies present in sera and nasal swabs from individuals infected with previously circulating strains or who were recently vaccinated, in comparison with a D614G reference virus. We utilized a new rapid neutralization assay, based on reporter cells that become positive for GFP after overnight infection. Sera from 58 convalescent individuals collected up to 9 months after symptoms, similarly neutralized B.1.1.7 and D614G. In contrast, after 9 months, convalescent sera had a mean sixfold reduction in neutralizing titers, and 40% of the samples lacked any activity against B.1.351. Sera from 19 individuals vaccinated twice with Pfizer Cominarty, longitudinally tested up to 6 weeks after vaccination, were similarly potent against B.1.1.7 but less efficacious against B.1.351, when compared to D614G. Neutralizing titers increased after the second vaccine dose, but remained 14-fold lower against B.1.351. In contrast, sera from convalescent or vaccinated individuals similarly bound the three spike proteins in a flow cytometry-based serological assay. Neutralizing antibodies were rarely detected in nasal swabs from vaccinees. Thus, faster-spreading SARS-CoV-2 variants acquired a partial resistance to neutralizing antibodies generated by natural infection or vaccination, which was most frequently detected in individuals with low antibody levels. Our results indicate that B1.351, but not B.1.1.7, may increase the risk of infection in immunized individuals."

Emerg Infect Dis: [Risk for International Importations of Variant SARS-CoV-2 Originating in the United Kingdom](#) (24 March 2021)

"A fast-spreading severe acute respiratory syndrome coronavirus 2 variant identified in the United Kingdom in December 2020 has raised international alarm. We analyzed data from 15 countries and estimated that the chance that this variant was imported into these countries by travelers from the United Kingdom by December 7 is >50%."

Chemotherapy: [SARS-CoV-2 Lineages and Sub-Lineages Circulating Worldwide: A Dynamic Overview](#) (18 March 2021)

"Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) originated in Wuhan, China, in early December 2019 has rapidly widespread worldwide, becoming one of the major global public health issues of the last centuries.

Over the course of the pandemic, due to the advanced whole-genome sequencing technologies, an unprecedented amount of genomes have been generated, providing invaluable insights into the ongoing evolution and epidemiology of the virus during the pandemic. Therefore, this large amount of data played an important role in the SARS-CoV-2 mitigation and control strategies.

The active monitoring and characterization of the SARS-CoV-2 lineages circulating worldwide is useful for a more specific diagnosis, better care, and timely treatment. In this review, a concise characterization of all the lineages and sub-lineages circulating and co-circulating across the world has been presented in order to determine the magnitude of the SARS-CoV-2 threat and to better understand the virus genetic diversity and its dispersion dynamics."

J Med Microbiol: [Profile of specific antibodies to the SARS-CoV-2](#) (18 March 2021)

"In this work, we studied the profile of IgM and IgG antibody responses to SARS-CoV-2 in 32 patients with COVID-19 from day 1 to day 24. IgM remained measurable for a much shorter period than IgG, suggesting that IgG antibody may represent the primary immune response."

## Vaccines and Vaccine Hesitancy

### *News in Brief*

The FDA has authorized Moderna to have up to 15 doses of coronavirus vaccine per vial; the label changes also allow for vials to be at room temperature for a longer period of 24 hours instead of 12 hours ([FDA](#); [BusinessWire](#)).

With older adults getting vaccinated, many new COVID-19 cases are happening in younger, unvaccinated adults ([ABC News](#)).

According to Michigan state officials, as many as 246 people considered fully vaccinated against COVID-19 were later diagnosed with the virus, with 3 deaths ([Detroit News](#)).

Russia has developed and registered the first COVID-19 vaccine for animals ([Al Jazeera](#)).

"Photos: The Great Vaccination Campaign" ([Atlantic](#)).

#9. "Nurses Gokalp Balli (left) and Bilge Koc, from the Gevas Public Health Center, vaccinate 74-year-old Basra Payza with the Sinovac Coronavac vaccine during a house call in the village of Daldere on February 12, 2021, in Van, Turkey. Medical teams across the country have been working house to house to administer the COVID-19 vaccine to elderly and vulnerable citizens." (Chris McGrath / Getty; used without permission)



### *Vaccine Effectiveness*

The Pfizer vaccine is 100% effective in adolescents (12-15 years old), according to new data from a Phase 3 trial by the company ([BusinessWire](#)).

The company also reported that the Pfizer vaccine remains 91% effective up to six months after the second dose, and is effective against the South Africa variant, B1351 ([Reuters](#); [Pfizer](#)).

The CDC has awarded a \$4.9 million grant to UCLA to study COVID-19 vaccine effectiveness in healthcare workers ([HPN](#)).

### *Adverse Reactions*

There are growing concerns about side effects (blood clots in particular) with the AstraZeneca vaccine ([Science](#); [STAT](#)).

"We need to talk about the AstraZeneca vaccine: For the moment, reports of a very rare, dangerous blood disorder among recipients cannot be ignored" ([Atlantic](#)).

The AZ vaccine isn't the only one of concern; the European Medicines Agency is investigating 4 'serious cases' of blood clots after the J&J vaccine ([Endpoints](#)).

The NIH is studying allergic reactions to the Moderna and Pfizer vaccines ([NIH](#)).

"Why is it so hard to investigate the rare side effects of COVID vaccines?" ([Nature](#))

### *Manufacturing the Vaccines*

An estimated 15 million doses of the Johnson & Johnson vaccine were contaminated by ingredients at a manufacturing plant in Baltimore; initial reports attribute it to human error and a review is underway ([WashPo](#)).

"Manufacturing moonshot: How Pfizer makes its millions of Covid-19 vaccine doses" ([CNN](#)).

"Keeping covid vaccines cold isn't easy. These ideas could help" ([MIT Tech Rev](#)).

The next vaccine could be a pill or nasal spray ([NPR](#)).

Long read: "The story of one dose: Inside the sprawling operational puzzle of bringing the Johnson & Johnson COVID vaccine to the public" ([Intelligencer](#)).

### *Peer-Reviewed Articles*

NEJM: [Antibody Persistence through 6 Months after the Second Dose of mRNA-1273 Vaccine for Covid-19](#) (06 April 2021)

"Interim results from a phase 3 trial of the Moderna mRNA-1273 severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccine indicated 94% efficacy in preventing coronavirus disease 2019 (Covid-19). The durability of protection is currently unknown. We describe mRNA1273-elicited binding and neutralizing antibodies in 33 healthy adult participants in an ongoing phase 1 trial, stratified according to age, at 180 days after the second dose of 100 µg (day 209)."

Nat Med: [Antibody responses to the BNT162b2 mRNA vaccine in individuals previously infected with SARS-CoV-2](#) (01 April 2021)

"In a cohort of BNT162b2 (Pfizer–BioNTech) mRNA vaccine recipients ( $n = 1,090$ ), we observed that spike-specific IgG antibody levels and ACE2 antibody binding inhibition responses elicited by a single vaccine dose in individuals with prior SARS-CoV-2 infection ( $n = 35$ ) were similar to those seen after two doses of vaccine in individuals without prior infection ( $n = 228$ ). Post-vaccine symptoms were more prominent for those with prior infection after the first dose, but symptomology was similar between groups after the second dose."

MMWR: [Interim Estimates of Vaccine Effectiveness of BNT162b2 and mRNA-1273 COVID-19 Vaccines in Preventing SARS-CoV-2 Infection Among Health Care Personnel, First Responders, and Other Essential and Frontline Workers — Eight U.S. Locations, December 2020–March 2021](#)  
(02 April 2021)

"What is already known about this topic? Messenger RNA (mRNA) COVID-19 vaccines have been shown to be effective in preventing symptomatic SARS-CoV-2 infection in randomized placebo-controlled Phase III trials.

What is added by this report? Prospective cohorts of 3,950 health care personnel, first responders, and other essential and frontline workers completed weekly SARS-CoV-2 testing for 13 consecutive weeks. Under real-world conditions, mRNA vaccine effectiveness of full immunization ( $\geq 14$  days after second dose) was 90% against SARS-CoV-2 infections regardless of symptom status; vaccine effectiveness of partial immunization ( $\geq 14$  days after first dose but before second dose) was 80%.

What are the implications for public health practice? Authorized mRNA COVID-19 vaccines are effective for preventing SARS-CoV-2 infection in real-world conditions. COVID-19 vaccination is recommended for all eligible persons."

J Eur Acad Dermatol Venereol: [Skin manifestations of the BNT162b2 mRNA COVID-19 vaccine in healthcare workers. "COVID-arm": a clinical and histological characterization](#) (30 March 2021)

"The coronavirus disease 2019 (COVID-19) has been associated to a wide clinical spectrum of skin manifestations, including chilblain-like, urticarial, vesicular, maculopapular, livedoid and vasculitic lesions, among others. However, the exact pathophysiology for the

appearance of skin lesions is still unknown. Several hypotheses have been suggested, including viral hypersensitivity reactions, overexpression of type I interferons, COVID-19 induced coagulopathy, thrombotic microangiopathy and direct viral damage."

Science: [mRNA vaccination boosts cross-variant neutralizing antibodies elicited by SARS-CoV-2 infection](#) (25 March 2021)

"Emerging SARS-CoV-2 variants have raised concerns about resistance to neutralizing antibodies elicited by previous infection or vaccination. We examined whether sera from recovered and naïve donors collected prior to, and following immunizations with existing mRNA vaccines, could neutralize the Wuhan-Hu-1 and B.1.351 variants. Pre-vaccination sera from recovered donors neutralized Wuhan-Hu-1 and sporadically neutralized B.1.351, but a single immunization boosted neutralizing titers against all variants and SARS-CoV-1 by up to 1000-fold. Neutralization was due to antibodies targeting the receptor binding domain and was not boosted by a second immunization. Immunization of naïve donors also elicited cross-neutralizing responses, but at lower titers. Our study highlights the importance of vaccinating both uninfected and previously infected persons to elicit cross-variant neutralizing antibodies."

## **Treatments and Management**

### ***News in Brief***

The NIH posted an update to treatment guidelines recommending monoclonal antibody cocktails (e.g., bamlanivimab plus etesevimab) but against bamlanivimab monotherapy ([NIH](#)).

Results from a Phase 3 study of lenzilumab, a humanized monoclonal antibody that targets CSF2/GM-CSF, suggest that the drug improves survival in COVID-19 patients without need for ventilation ([Humanigen](#)).

Eli Lilly's baricitinib (JAK inhibitor) did not show statistically significant benefit at keeping COVID-19 patients from progressing to ventilation ([Lilly](#)).

### ***Peer-Reviewed Articles***

Lancet Regional Health: [A randomized, double-blind, placebo-controlled phase 1 trial of inhaled and intranasal niclosamide: A broad spectrum antiviral candidate for treatment of COVID-19](#) (06 April 2021)

"Coronavirus disease 19 (COVID-19) is spreading globally and treatment options remain limited. A formulation of niclosamide, a potent anti-SARS-CoV-2 agent and a broad-

spectrum antiviral treatment candidate, optimized for inhalation and intranasal administration (UNI91104) was developed.

We conducted a randomized, placebo-controlled, double-blind, single-centre, dose-ascending Phase 1 trial to assess the safety of UNI91104 in Denmark (NCT04576312). Healthy volunteers were randomly assigned to a ascending single dose in cohort 1–4 and five doses over 2.5 days in cohort 5. Inclusion criteria included a minimum 80% of predicted lung function. Exclusion criteria included severe, clinically significant allergies and current acute or chronic condition especially airway diseases. Safety was evaluated through adverse events (AEs) and pulmonary function tests including forced expiratory volume in one second (FEV1) and fractional exhaled nitric oxide (FeNO) tests. The primary endpoints were defined as the frequency of reported AEs and the change of safety variables relative to pre-dose. Data from all enroled healthy volunteers receiving any amount of IMP was included in the primary analyses. The pharmacokinetics of UNI91104 was determined.

The trial was conducted between 29 June 2020 and 08 August 2020. Thirty-four healthy volunteers received UNI91104 and ten placebo. No serious AEs or discontinuation were reported. Mild irritation in the upper respiratory tract following inhalation of UNI91104 was reported as most frequent AE (45 events in 26 healthy volunteers, 59% of all healthy volunteers). Nasal application was well-tolerated. There was no evidence of difference in the change of mean levels of pulmonary function tests between active and placebo group across all cohorts. Five healthy volunteers (11.4%) (1 on placebo) had signs of increased transient FeNO and 4 on active (9.1%) experienced asymptomatic drops in FEV1, which resolved spontaneously or were reversible with a  $\beta$ 2-agonist. Niclosamide exhibited dose-proportional pharmacokinetics following inhalation and intranasal administration.

UNI91104, a promising candidate for inhalation and intranasal therapy against COVID-19 and other viral respiratory tract infections is well-tolerated in healthy volunteers and warrants further testing in patient trials."

JAMA Intern Med: [Incidence of 30-Day Venous Thromboembolism in Adults Tested for SARS-CoV-2 Infection in an Integrated Health Care System in Northern California](#) (05 April 2021)

"This cohort study examines the 30-day incidence of outpatient and hospital-associated venous thromboembolism following SARS-CoV-2 testing among adults in a large health system."

JAMA Netw Open: [Mortality and Readmission Rates Among Patients With COVID-19 After Discharge From Acute Care Setting With Supplemental Oxygen](#) (01 April 2021)

"Question: What are the mortality and readmission rates in patients with COVID-19 pneumonia discharged according to an expected practice approach with supplemental home oxygen?

**Findings:** In this cohort study of 621 patients with COVID-19 discharged with supplemental home oxygen from emergency department and inpatient encounters at 2 large urban medical centers, the all-cause mortality rate was 1.3% and the all-cause 30-day return hospital admission rate was 8.5%. No patients died in the ambulatory setting or in transit when returning to acute care setting.

**Meaning:** In this study, a careful and systematic expected practice approach to treatment of patients with COVID-19 using home oxygen was associated with low all-cause mortality and low 30-day return admission rates."

**JAMA [Association Between Renin-Angiotensin-Aldosterone System Inhibitors and Clinical Outcomes in Patients With COVID-19: A Systematic Review and Meta-analysis](#) (31 March 2021)**

"Question: Is the receipt of angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin receptor blockers (ARBs) associated with worse clinical outcomes among patients with COVID-19?

**Findings:** In this systematic review and meta-analysis of 52 studies that evaluated clinical outcomes among 101 949 total patients with COVID-19 who did and did not receive ACEIs or ARBs, a significantly lower risk of multivariable-adjusted mortality and severe adverse events was found among patients who received ACEIs or ARBs compared with patients who did not. A subgroup analysis of patients with hypertension indicated significant decreases in mortality and severe adverse events among patients receiving ACEIs or ARBs in both unadjusted and adjusted analyses.

**Meaning:** The study's findings suggest that ACEIs and ARBs may be associated with protective benefits for patients with COVID-19 and that patients may continue receiving ACEIs and ARBs for the treatment of any condition without an increased risk of worse outcomes unless specifically advised to avoid them by treating clinicians."

## **Pre-Existing Conditions, Comorbidities, and Impact on Other Diseases**

### ***Peer-Reviewed Articles***

**EClinicalMedicine: [The relationship of large city out-of-hospital cardiac arrests and the prevalence of COVID-19](#) (07 April 2021)**

"Though variable, many major metropolitan cities reported profound and unprecedented increases in out-of-hospital cardiac arrest (OHCA) in early 2020. This study examined the relative magnitude of those increases and their relationship to COVID-19 prevalence.

EMS (9-1-1 system) medical directors for 50 of the largest U.S. cities agreed to provide the aggregate, de-identified, pre-existing monthly tallies of OHCA among adults (age >18 years)

occurring between January and June 2020 within their respective jurisdictions. Identical comparison data were also provided for corresponding time periods in 2018 and 2019. Equivalent data were obtained from the largest cities in Italy, United Kingdom and France, as well as Perth, Australia and Auckland, New Zealand.

Significant OHCA escalations generally paralleled local prevalence of COVID-19. During April, most U.S. cities (34/50) had >20% increases in OHCA versus 2018–2019 which reflected high local COVID-19 prevalence. Thirteen observed 1.5-fold increases in OHCA and three COVID-19 epicenters had >100% increases (2.5-fold in New York City). Conversely, cities with lesser COVID-19 impact observed unchanged (or even diminished) OHCA numbers. Altogether (n = 50), on average, OHCA cases/city rose 59% during April (p = 0.03). By June, however, after mitigating COVID-19 spread, cities with the highest OHCA escalations returned to (or approached) pre-COVID OHCA numbers while cities minimally affected by COVID-19 during April (and not experiencing OHCA increases), then had marked OHCA escalations when COVID-19 began to surge locally. European, Australian, and New Zealand cities mirrored the U.S. experience.

Most metropolitan cities experienced profound escalations of OHCA generally paralleling local prevalence of COVID-19. Most of these patients were pronounced dead without COVID-19 testing."

Lancet Respir Med: [Association between pre-existing respiratory disease and its treatment, and severe COVID-19: a population cohort study](#) (01 April 2021)

"Previous studies suggested that the prevalence of chronic respiratory disease in patients hospitalised with COVID-19 was lower than its prevalence in the general population. The aim of this study was to assess whether chronic lung disease or use of inhaled corticosteroids (ICS) affects the risk of contracting severe COVID-19.

In this population cohort study, records from 1205 general practices in England that contribute to the QResearch database were linked to Public Health England's database of SARS-CoV-2 testing and English hospital admissions, intensive care unit (ICU) admissions, and deaths for COVID-19. All patients aged 20 years and older who were registered with one of the 1205 general practices on Jan 24, 2020, were included in this study. With Cox regression, we examined the risks of COVID-19-related hospitalisation, admission to ICU, and death in relation to respiratory disease and use of ICS, adjusting for demographic and socioeconomic status and comorbidities associated with severe COVID-19.

Between Jan 24 and April 30, 2020, 8 256 161 people were included in the cohort and observed, of whom 14 479 (0.2%) were admitted to hospital with COVID-19, 1542 (<0.1%) were admitted to ICU, and 5956 (0.1%) died. People with some respiratory diseases were at an increased risk of hospitalisation (chronic obstructive pulmonary disease [COPD] hazard ratio [HR] 1.54 [95% CI 1.45–1.63], asthma 1.18 [1.13–1.24], severe asthma 1.29 [1.22–1.37;

people on three or more current asthma medications], bronchiectasis 1·34 [1·20–1·50], sarcoidosis 1·36 [1·10–1·68], extrinsic allergic alveolitis 1·35 [0·82–2·21], idiopathic pulmonary fibrosis 1·59 [1·30–1·95], other interstitial lung disease 1·66 [1·30–2·12], and lung cancer 2·24 [1·89–2·65]) and death (COPD 1·54 [1·42–1·67], asthma 0·99 [0·91–1·07], severe asthma 1·08 [0·98–1·19], bronchiectasis 1·12 [0·94–1·33], sarcoidosis 1·41 [0·99–1·99], extrinsic allergic alveolitis 1·56 [0·78–3·13], idiopathic pulmonary fibrosis 1·47 [1·12–1·92], other interstitial lung disease 2·05 [1·49–2·81], and lung cancer 1·77 [1·37–2·29]) due to COVID-19 compared with those without these diseases. Admission to ICU was rare, but the HR for people with asthma was 1·08 (0·93–1·25) and severe asthma was 1·30 (1·08–1·58). In a post-hoc analysis, relative risks of severe COVID-19 in people with respiratory disease were similar before and after shielding was introduced on March 23, 2020. In another post-hoc analysis, people with two or more prescriptions for ICS in the 150 days before study start were at a slightly higher risk of severe COVID-19 compared with all other individuals (ie, no or one ICS prescription): HR 1·13 (1·03–1·23) for hospitalisation, 1·63 (1·18–2·24) for ICU admission, and 1·15 (1·01–1·31) for death.

The risk of severe COVID-19 in people with asthma is relatively small. People with COPD and interstitial lung disease appear to have a modestly increased risk of severe disease, but their risk of death from COVID-19 at the height of the epidemic was mostly far lower than the ordinary risk of death from any cause. Use of inhaled steroids might be associated with a modestly increased risk of severe COVID-19."

PLoS One: [Patient access to chronic medications during the Covid-19 pandemic: Evidence from a comprehensive dataset of US insurance claims](#) (01 April 2021)

"Patient access and adherence to chronic medications is critical. In this work, we evaluate whether disruptions related to Covid-19 have affected new and existing patients' access to pharmacological therapies without interruption. We do so by performing a retrospective analysis on a dataset of 9.4 billion US prescription drug claims from 252 million patients from May, 2019 through August, 2020 (about 93% of prescriptions dispensed within those months). Using fixed effect (conditional likelihood) linear models, we evaluate continuity of care, how many days of supply patients received, and the likelihood of discontinuing therapy for drugs from classes with significant population health impacts. Findings indicate that more prescriptions were filled in March 2020 than in any prior month, followed by a significant drop in monthly dispensing. Compared to the pre-Covid era, a patient's likelihood of discontinuing some medications increased after the spread of Covid: norgestrel-ethynodiol estradiol (hormonal contraceptive) discontinuation increased 0.62% (95% CI: 0.59% to 0.65%,  $p<0.001$ ); dexamethasone HCL (ADHD stimulant treatment) discontinuation increased 2.84% (95% CI: 2.79% to 2.89%,  $p<0.001$ ); escitalopram oxalate (SSRI antidepressant) discontinuation increased 0.57% (95% CI: 0.561% to 0.578%,  $p<0.001$ ); and haloperidol (antipsychotic) discontinuation increased 1.49% (95% CI: 1.41% to 1.57%,

p<0.001). In contrast, the likelihood of discontinuing tacrolimus (immunosuppressant) decreased 0.15% (95% CI: 0.12% to 0.19%, p<0.001). The likelihood of discontinuing buprenorphine/naloxone (opioid addiction therapy) decreased 0.59% (95% CI: 0.55% to 0.62% decrease, p<0.001). We also observe a notable decline in new patients accessing these latter two therapies. Most US patients were able to access chronic medications during the early months of Covid-19, but still were more likely to discontinue their therapies than in previous months. Further, fewer than normal new patients started taking medications that may be vital to their care. Providers would do well to inquire about adherence and provide prompt, nonjudgmental, re-initiation of medications. From a policy perspective, opioid management programs seem to demonstrate a robust ability to manage existing patients in spite of disruption."

Thorax: [Decrease in hospital admissions for respiratory diseases during the COVID-19 pandemic: a nationwide claims study](#) (29 March 2021)

"Non-pharmaceutical interventions (NPIs) have been widely implemented to mitigate the spread of COVID-19. We assessed the effect of NPIs on hospitalisations for pneumonia, influenza, COPD and asthma. This retrospective, ecological study compared the weekly incidence of hospitalisation for four respiratory conditions before (January 2016–January 2020) and during (February–July 2020) the implementation of NPI against COVID-19. Hospitalisations for all four respiratory conditions decreased substantially during the intervention period. The cumulative incidence of admissions for COPD and asthma was 58% and 48% of the mean incidence during the 4 preceding years, respectively.

This article is made freely available for use in accordance with BMJ's website terms and conditions for the duration of the covid-19 pandemic or until otherwise determined by BMJ. You may use, download and print the article for any lawful, non-commercial purpose (including text and data mining) provided that all copyright notices and trade marks are retained."

Thorax: [Impact of COVID-19 lockdown on emergency asthma admissions and deaths: national interrupted time series analyses for Scotland and Wales](#) (29 March 2021)

"Using data from Public Health Scotland and the Secure Anonymised Information Linkage Databank in Wales, we compared weekly counts of emergency admissions and deaths due to asthma over the first 18 weeks in 2020 with the national averages over 2015–2019. We modelled the impact of instigating lockdown on these outcomes using interrupted time-series analysis. Using fixed-effect meta-analysis, we derived pooled estimates of the overall changes in trends across the two nations. We also investigated trends in asthma-related primary care prescribing and emergency department (ED) attendances in Wales.

Lockdown was associated with a 36% pooled reduction in emergency admissions for asthma (incidence rate ratio, IRR: 0.64, 95% CI: 0.49 to 0.83, p value 0.001) across both countries.

There was no significant change in asthma deaths (pooled IRR: 0.57, 95% CI: 0.17 to 1.94, p value 0.37). ED asthma attendances in Wales declined during lockdown (IRR: 0.85, 95% CI: 0.73 to 0.99, p value 0.03). A large spike of 121% more inhaled corticosteroids and 133% more oral corticosteroid prescriptions was seen in Wales in the week before lockdown.

National lockdowns were associated with substantial reductions in severe asthma exacerbations leading to hospital admission across both Scotland and Wales, with no corresponding increase in asthma deaths."

Thorax: [Impact of COVID-19 national lockdown on asthma exacerbations: interrupted time-series analysis of English primary care data](#) (29 March 2021)

"We conducted an interrupted time-series (lockdown on 23 March 2020 as point of interruption) analysis in asthma cohort identified using a validated algorithm from a national-level primary care database, the Optimum Patient Care Database. We derived asthma exacerbation rates for every week and compared exacerbation rates in the period: January to August 2020 with a pre-COVID-19 period and January to August 2016–2019. Exacerbations were defined as asthma-related hospital attendance/admission (including accident and emergency visit), or an acute course of oral corticosteroids with evidence of respiratory review, as recorded in primary care. We used a generalised least squares modelling approach and stratified the analyses by age, sex, English region and healthcare setting.

From a database of 9 949 387 patients, there were 100 165 patients with asthma who experienced at least one exacerbation during 2016–2020. Of 278 996 exacerbation episodes, 49 938 (17.9%) required hospital visit. Comparing pre-lockdown to post-lockdown period, we observed a statistically significant reduction in the level ( $-0.196$  episodes per person-year;  $p<0.001$ ; almost 20 episodes for every 100 patients with asthma per year) of exacerbation rates across all patients. The reductions in level in stratified analyses were: 0.005–0.244 (healthcare setting, only those without hospital attendance/admission were significant), 0.210–0.277 (sex), 0.159–0.367 (age), 0.068–0.590 (region).

There has been a significant reduction in attendance to primary care for asthma exacerbations during the pandemic. This reduction was observed in all age groups, both sexes and across most regions in England."

JAMA Psychiatry: [How COVID-19 Affects the Brain](#) (26 March 2021)

"This article discusses possible pathogenic mechanisms of brain dysfunction in patients with COVID-19."

Ophthalmology: [Comparison of the myopic progression before, during and after COVID-19 lockdown](#) (23 March 2021)

"Researchers from the Eye Hospital and School of Ophthalmology and Optometry at Wenzhou Medical University and the National Clinical Research Center for Ocular Diseases in Wenzhou, Zhejiang, China conducted an analysis of 29,719 junior high students in Hangzhou, China participating in the cohort study, Myopia Screening Survey Of Children and Teenagers In Schools (MYOSOTIS), examining their corrected and non-corrected visual acuity (VA) and change in spherical equivalent refraction (SER) during the COVID-19 lockdown. They found an accelerated reversible myopic progression during different rounds of the lockdown (Figure 1), which they speculate is from accumulative spasms, and suggest further consideration and management for this condition in children and teenagers in the setting of future lockdowns." (summary from [April 2 COVID-19 LST](#))

Ann Oncol: [Association of Clinical Factors and Recent Anti-Cancer Therapy with COVID-19 Severity among Patients with Cancer: A Report from the COVID-19 and Cancer Consortium](#) (19 March 2021)

"Patients with cancer may be at high risk of adverse outcomes from SARS-CoV-2 infection. We analyzed a cohort of patients with cancer and COVID-19 reported to the COVID-19 and Cancer Consortium (CCC19) to identify prognostic clinical factors, including laboratory measurements and anti-cancer therapies.

Patients with active or historical cancer and a laboratory-confirmed SARS-CoV-2 diagnosis recorded between March 17–November 18, 2020 were included. The primary outcome was COVID-19 severity measured on an ordinal scale (uncomplicated, hospitalized, admitted to intensive care unit, mechanically ventilated, died within 30 days). Multivariable regression models included demographics, cancer status, anti-cancer therapy and timing, COVID-19-directed therapies, and laboratory measurements (among hospitalized patients).

4,966 patients were included (median age 66 years, 51% female, 50% non-Hispanic white); 2,872 (58%) were hospitalized and 695 (14%) died; 61% had cancer that was present, diagnosed, or treated within the year prior to COVID-19 diagnosis. Older age, male sex, obesity, cardiovascular and pulmonary comorbidities, renal disease, diabetes mellitus, non-Hispanic Black race, Hispanic ethnicity, worse ECOG performance status, recent cytotoxic chemotherapy, and hematologic malignancy were associated with higher COVID-19 severity. Among hospitalized patients, low or high absolute lymphocyte count, high absolute neutrophil count, low platelet count, abnormal creatinine, troponin, LDH, and CRP were associated with higher COVID-19 severity. Patients diagnosed early in the COVID-19 pandemic (January–April 2020) had worse outcomes than those diagnosed later. Specific anti-cancer therapies (e.g. R-CHOP, platinum combined with etoposide, and DNA methyltransferase inhibitors) were associated with high 30-day all-cause mortality.

Clinical factors (e.g. older age, hematological malignancy, recent chemotherapy) and laboratory measurements were associated with poor outcomes among patients with cancer

and COVID-19. Although further studies are needed, caution may be required in utilizing particular anti-cancer therapies."

Colorectal Dis: [Delay to elective colorectal cancer surgery and implications for survival: a systematic review and meta-analysis](#) (13 March 2021)

"The Covid-19 pandemic has delayed elective colorectal cancer (CRC) surgery. The aim of this study was to see whether or not this may affect overall survival (OS) and disease-free survival (DFS).

A systematic review was carried out according to PRISMA guidelines (PROSPERO ID: CRD42020189158). Medline, EMBASE and Scopus were interrogated. Patients aged over 18 years with a diagnosis of colon or rectal cancer who received elective surgery as their primary treatment were included. Delay to elective surgery was defined as the period between CRC diagnosis and the day of surgery. Meta-analysis of the outcomes OS and DFS were conducted. Forest plots, funnel plots and tests of heterogeneity were produced. An estimated number needed to harm (NNH) was calculated for statistically significant pooled hazard ratios (HRs).

Of 3753 articles identified, seven met the inclusion criteria. Encompassing 314 560 patients, three of the seven studies showed that a delay to elective resection is associated with poorer OS or DFS. OS was assessed at a 1 month delay, the HR for six datasets was 1.13 (95% CI 1.02–1.26,  $p = 0.020$ ) and at 3 months the pooled HR for three datasets was 1.57 (95% CI 1.16–2.12,  $p = 0.004$ ). The estimated NNH for a delay at 1 month and 3 months was 35 and 10 respectively. Delay was nonsignificantly negatively associated with DFS on meta-analysis.

This review recommends that elective surgery for CRC patients is not postponed longer than 4 weeks, as available evidence suggests extended delays from diagnosis are associated with poorer outcomes. Focused research is essential so patient groups can be prioritized based on risk factors in future delays or pandemics."

## Long COVID / Post-COVID Period

### ***News in Brief***

"People are losing their taste and smell to covid-19. Now there's a cookbook to help" ([WashPo](#)).

Got COVID brain fog? This video game might help ([BusinessWire](#)).

### **Peer-Reviewed Articles**

#### **Lancet Psychiatry: [6-month neurological and psychiatric outcomes in 236 379 survivors of COVID-19: a retrospective cohort study using electronic health records](#) (06 April 2021)**

"To our knowledge, we provide the first meaningful estimates of the risks of major neurological and psychiatric conditions in the 6 months after a COVID-19 diagnosis, using the electronic health records of over 236 000 patients with COVID-19. We report their incidence and hazard ratios compared with patients who had had influenza or other respiratory tract infections. We show that both incidence and hazard ratios were greater in patients who required hospitalisation or admission to the intensive therapy unit (ITU), and in those who had encephalopathy (delirium and other altered mental states) during the illness compared with those who did not.

COVID-19 was robustly associated with an increased risk of neurological and psychiatric disorders in the 6 months after a diagnosis. Given the size of the pandemic and the chronicity of many of the diagnoses and their consequences (eg, dementia, stroke, and intracranial haemorrhage), substantial effects on health and social care systems are likely to occur. Our data provide important evidence indicating the scale and nature of services that might be required. The findings also highlight the need for enhanced neurological follow-up of patients who were admitted to ITU or had encephalopathy during their COVID-19 illness."

#### **J Infect Dis: [Inflammatory profiles and clinical features of COVID-19 survivors three months after discharge in Wuhan, China](#) (04 April 2021)**

"Post-discharge immunity and its correlation with clinical features among patients recovered from COVID-19 are poorly described. This prospective cross-sectional study explored the inflammatory profiles and clinical recovery of COVID-19 patients at 3 months post-discharge.

COVID-19 patients discharged from four hospitals in Wuhan, recovered asymptomatic patients (APs) from an isolation hotel, and uninfected healthy controls (HCs) were recruited. Viral nucleic acid and antibody detection, laboratory examination, computed tomography, pulmonary function assessment, multiplex cytokine assay, and flow cytometry were performed.

The 72 age-, sex- and body mass index-matched participants included 19 severe/critical patients (SPs), 20 mild/moderate patients (MPs), 16 APs, and 17 HCs. At 3 months after discharge, levels of pro-inflammatory cytokines and factors related to vascular injury/repair in recovered COVID-19 patients had not returned to those of the HCs, especially among recovered SPs compared to recovered MPs and APs. These cytokines were significantly correlated with impaired pulmonary function and chest CT abnormalities. However, levels

of immune cells had returned to nearly normal levels and were not significantly correlated with abnormal clinical features.

Vascular injury, inflammation, and chemotaxis persisted in COVID-19 patients and were correlated with abnormal clinical features 3 months after discharge, especially in recovered SPs."

BMJ: [Post-covid syndrome in individuals admitted to hospital with covid-19: retrospective cohort study](#) (31 March 2021)

"Objective: To quantify rates of organ specific dysfunction in individuals with covid-19 after discharge from hospital compared with a matched control group from the general population.

Participants: 47 780 individuals (mean age 65, 55% men) in hospital with covid-19 and discharged alive by 31 August 2020, exactly matched to controls from a pool of about 50 million people in England for personal and clinical characteristics from 10 years of electronic health records.

Main outcome measures: Rates of hospital readmission (or any admission for controls), all cause mortality, and diagnoses of respiratory, cardiovascular, metabolic, kidney, and liver diseases until 30 September 2020. Variations in rate ratios by age, sex, and ethnicity.

Results: Over a mean follow-up of 140 days, nearly a third of individuals who were discharged from hospital after acute covid-19 were readmitted (14 060 of 47 780) and more than 1 in 10 (5875) died after discharge, with these events occurring at rates four and eight times greater, respectively, than in the matched control group. Rates of respiratory disease ( $P<0.001$ ), diabetes ( $P<0.001$ ), and cardiovascular disease ( $P<0.001$ ) were also significantly raised in patients with covid-19, with 770 (95% confidence interval 758 to 783), 127 (122 to 132), and 126 (121 to 131) diagnoses per 1000 person years, respectively. Rate ratios were greater for individuals aged less than 70 than for those aged 70 or older, and in ethnic minority groups compared with the white population, with the largest differences seen for respiratory disease (10.5 (95% confidence interval 9.7 to 11.4) for age less than 70 years v 4.6 (4.3 to 4.8) for age  $\geq 70$ , and 11.4 (9.8 to 13.3) for non-white v 5.2 (5.0 to 5.5) for white individuals).

Conclusions: Individuals discharged from hospital after covid-19 had increased rates of multiorgan dysfunction compared with the expected risk in the general population. The increase in risk was not confined to the elderly and was not uniform across ethnicities. The diagnosis, treatment, and prevention of post-covid syndrome requires integrated rather than organ or disease specific approaches, and urgent research is needed to establish the risk factors."

EClinicalMedicine: [Understanding the survivorship burden of long COVID](#) (25 February 2021)

"Emerging evidence suggests that upwards of 20% of all SARS-CoV-2 positive individuals continue to experience chronic and debilitating symptoms, known either as 'long COVID' or 'post COVID syndrome', following the resolution of their initial infection. Despite this sizeable cohort, there have been limited coordinated attempts to understand the overall survivorship burden associated with this condition....

Despite its predominant use in oncological literature, we can draw several parallels between the journey of long COVID and many cancers; both patient cohorts typically describe (i) the psychological impact of an unexpected diagnosis and duration of symptoms; (ii) a complex set of evolving physical symptoms; (iii) on-going changes in physical function; and (iv) an associated change in lifestyle, finances and interpersonal relationships."

## Pregnancy and Perinatal Care

### *Peer-Reviewed Articles*

Lancet Glob Health: [Effects of the COVID-19 pandemic on maternal and perinatal outcomes: a systematic review and meta-analysis](#) (31 March 2021)

"We did a systematic review and meta-analysis of studies on the effects of the pandemic on maternal, fetal, and neonatal outcomes. We searched MEDLINE and Embase in accordance with PRISMA guidelines, from Jan 1, 2020, to Jan 8, 2021, for case-control studies, cohort studies, and brief reports comparing maternal and perinatal mortality, maternal morbidity, pregnancy complications, and intrapartum and neonatal outcomes before and during the pandemic. We also planned to record any additional maternal and offspring outcomes identified. Studies of solely SARS-CoV-2-infected pregnant individuals, as well as case reports, studies without comparison groups, narrative or systematic literature reviews, preprints, and studies reporting on overlapping populations were excluded. Quantitative meta-analysis was done for an outcome when more than one study presented relevant data. Random-effects estimate of the pooled odds ratio (OR) of each outcome were generated with use of the Mantel-Haenszel method. This review was registered with PROSPERO (CRD42020211753).

The search identified 3592 citations, of which 40 studies were included. We identified significant increases in stillbirth (pooled OR 1.28 [95% CI 1.07–1.54]; I<sup>2</sup>=63%; 12 studies, 168 295 pregnancies during and 198 993 before the pandemic) and maternal death (1.37 [1.22–1.53; I<sup>2</sup>=0%, two studies [both from low-income and middle-income countries], 1 237 018 and 2 224 859 pregnancies) during versus before the pandemic. Preterm births before 37 weeks' gestation were not significantly changed overall (0.94 [0.87–1.02]; I<sup>2</sup>=75%; 15 studies, 170 640 and 656 423 pregnancies) but were decreased in high-income countries

(0.91 [0.84–0.99]; I<sup>2</sup>=63%; 12 studies, 159 987 and 635 118 pregnancies), where spontaneous preterm birth was also decreased (0.81 [0.67–0.97]; two studies, 4204 and 6818 pregnancies). Mean Edinburgh Postnatal Depression Scale scores were higher, indicating poorer mental health, during versus before the pandemic (pooled mean difference 0.42 [95% CI 0.02–0.81; three studies, 2330 and 6517 pregnancies]. Surgically managed ectopic pregnancies were increased during the pandemic (OR 5.81 [2.16–15.6]; I<sup>2</sup>=26%; three studies, 37 and 272 pregnancies). No overall significant effects were identified for other outcomes included in the quantitative analysis: maternal gestational diabetes; hypertensive disorders of pregnancy; preterm birth before 34 weeks', 32 weeks', or 28 weeks' gestation; iatrogenic preterm birth; labour induction; modes of delivery (spontaneous vaginal delivery, caesarean section, or instrumental delivery); post-partum haemorrhage; neonatal death; low birthweight (<2500 g); neonatal intensive care unit admission; or Apgar score less than 7 at 5 min.

Global maternal and fetal outcomes have worsened during the COVID-19 pandemic, with an increase in maternal deaths, stillbirth, ruptured ectopic pregnancies, and maternal depression. Some outcomes show considerable disparity between high-resource and low-resource settings. There is an urgent need to prioritise safe, accessible, and equitable maternity care within the strategic response to this pandemic and in future health crises."

AJOG: [COVID-19 vaccine response in pregnant and lactating women: a cohort study](#) (25 March 2021)

"Pregnant and lactating women were excluded from initial COVID-19 vaccine trials; thus, data to guide vaccine decision-making are lacking.

To evaluate the immunogenicity and reactogenicity of COVID-19 mRNA vaccination in pregnant and lactating women compared to: (1) non-pregnant controls and (2) natural COVID-19 infection in pregnancy.

131 reproductive-age vaccine recipients (84 pregnant, 31 lactating, and 16 non-pregnant) were enrolled in a prospective cohort study at two academic medical centers. Titers of SARS-CoV-2 Spike and RBD IgG, IgA and IgM were quantified in participant sera (N=131) and breastmilk (N=31) at baseline, second vaccine dose, 2–6 weeks post second vaccine, and at delivery by Luminex. Umbilical cord sera (N=10) titers were assessed at delivery. Titers were compared to those of pregnant women 4–12 weeks from natural infection (N=37) by ELISA. A pseudovirus neutralization assay was used to quantify neutralizing antibody titers for the subset of women who delivered during the study period. Post-vaccination symptoms were assessed via questionnaire. Kruskal-Wallis tests and a mixed effects model, with correction for multiple comparisons, were used to assess differences between groups.

Vaccine-induced antibody titers were equivalent in pregnant and lactating compared to non-pregnant women (median [IQR] 5.59 [4.68–5.89] pregnant, 5.74 [5.06–6.22] lactating,

5.62 [4.77-5.98] non-pregnant,  $p = 0.24$ ). All titers were significantly higher than those induced by SARS-CoV-2 infection during pregnancy ( $p < 0.0001$ ). Vaccine-generated antibodies were present in all umbilical cord blood and breastmilk samples. Neutralizing antibody titers were lower in umbilical cord compared to maternal sera, although this finding did not achieve statistical significance (median [IQR] 104.7 [61.2-188.2] maternal sera, 52.3 [11.7-69.6] cord sera,  $p=0.05$ ). The second vaccine dose (boost dose) increased SARS-CoV-2-specific IgG, but not IgA, in maternal blood and breastmilk. No differences were noted in reactogenicity across the groups.

COVID-19 mRNA vaccines generated robust humoral immunity in pregnant and lactating women, with immunogenicity and reactogenicity similar to that observed in non-pregnant women. Vaccine-induced immune responses were significantly greater than the response to natural infection. Immune transfer to neonates occurred via placenta and breastmilk."

## Pediatric Population

### ***Peer-Reviewed Articles***

PNAS: [Learning loss due to school closures during the COVID-19 pandemic](#) (07 April 2021)

"Suspension of face-to-face instruction in schools during the COVID-19 pandemic has led to concerns about consequences for students' learning. So far, data to study this question have been limited. Here we evaluate the effect of school closures on primary school performance using exceptionally rich data from The Netherlands ( $n \approx 350,000$ ). We use the fact that national examinations took place before and after lockdown and compare progress during this period to the same period in the 3 previous years. The Netherlands underwent only a relatively short lockdown (8 wk) and features an equitable system of school funding and the world's highest rate of broadband access. Still, our results reveal a learning loss of about 3 percentile points or 0.08 standard deviations. The effect is equivalent to one-fifth of a school year, the same period that schools remained closed. Losses are up to 60% larger among students from less-educated homes, confirming worries about the uneven toll of the pandemic on children and families. Investigating mechanisms, we find that most of the effect reflects the cumulative impact of knowledge learned rather than transitory influences on the day of testing. Results remain robust when balancing on the estimated propensity of treatment and using maximum-entropy weights or with fixed-effects specifications that compare students within the same school and family. The findings imply that students made little or no progress while learning from home and suggest losses even larger in countries with weaker infrastructure or longer school closures."

JAMA Ophthalmol: [Ocular Assessments of a Series of Newborns Gestationally Exposed to Maternal COVID-19 Infection](#) (07 April 2021)

"Question: What are the ophthalmological manifestations in newborns after maternal COVID-19 infection?

Findings: In this case series, 165 newborns exposed to SARS-CoV-2 went through ophthalmological evaluation. One exposed newborn presented with retinal vascular tortuosity and venous engorgement seen on ophthalmoscopy, 7 newborns showed intraretinal hemorrhages, and 2 newborns had retinopathy of prematurity.

Meaning: These findings likely rule out a moderate or high increased risk of ocular involvement in newborns of mothers with SARS-CoV-2 infection regardless of gestational age."

JAMA Netw Open: [Assessment of Pediatric Admissions for Kawasaki Disease or Infectious Disease During the COVID-19 State of Emergency in Japan](#) (06 April 2021)

"Question: Is Kawasaki disease (KD) associated with droplet- or contact-transmitted infection?

Findings: In this cross-sectional study of 17 235 pediatric patients, the number of admissions for KD showed no significant change (27.4% decrease) during quarantine owing to the COVID-19 pandemic, whereas there were significant decreases in numbers of hospital admissions for droplet-transmitted or contact-transmitted respiratory tract infections (75.3% decrease) and gastrointestinal infections (86.3% decrease). Thus, the ratio of KD admissions to admissions for these infections increased.

Meaning: These findings suggest that contact or droplet transmission is not a major route for KD development and that KD may be associated with airborne disease."

See also: [invited commentary](#)

JAMA Netw Open: [Trends in Geographic and Temporal Distribution of US Children With Multisystem Inflammatory Syndrome During the COVID-19 Pandemic](#) (06 April 2021)

"Question: What are the clinical characteristics and geographic and temporal distribution of multisystem inflammatory syndrome in children (MIS-C) in the United States?

Findings: In this cross-sectional study, 1733 patients with MIS-C were identified with predominantly gastrointestinal, mucocutaneous, and cardiovascular manifestations, and a majority required intensive care. MIS-C peaks closely followed the peaks of COVID-19 and the spread of the pandemic from urban to rural communities.

Meaning: The data are consistent with observations that MIS-C resulted from delayed immunologic responses to infection by SARS-CoV-2."

See also: [editorial](#)

JAMA Pediatr: [Estimates and Projections of COVID-19 and Parental Death in the US](#) (05 April 2021)

"This study estimates the expected number of affected children for each COVID-19 death....

Our model suggests that each COVID-19 death leaves 0.078 children aged 0 to 17 parentally bereaved. This represents a 17.5% to 20.2% increase in parental bereavement absent COVID-19. Although the bereavement multiplier is small, it translates into large numbers of children who have lost a parent....

The number of children experiencing a parent dying of COVID-19 is staggering, with an estimated 37 300 to 43 000 already affected."

## **Mental Health and Wellness**

### ***Peer-Reviewed Articles***

JAMA Netw Open: [Association of Symptoms of Posttraumatic Stress Disorder With Posttraumatic Psychological Growth Among US Veterans During the COVID-19 Pandemic](#) (08 April 2021)

"This survey study uses self-reported data from the 2019-2020 National Health and Resilience in Veterans Study to assess the association of symptoms of posttraumatic stress disorder (PTSD) with posttraumatic psychological growth among US veterans during the COVID-19 pandemic."

MMWR: [Symptoms of Anxiety or Depressive Disorder and Use of Mental Health Care Among Adults During the COVID-19 Pandemic — United States, August 2020–February 2021](#) (02 April 2021)

"What is already known about this topic? Large disease outbreaks have been associated with mental health problems.

What is added by this report? During August 2020–February 2021, the percentage of adults with recent symptoms of an anxiety or a depressive disorder increased from 36.4% to 41.5%, and the percentage of those reporting an unmet mental health care need increased from 9.2% to 11.7%. Increases were largest among adults aged 18–29 years and those with less than a high school education.

What are the implications for public health practice? Trends in mental health can be used to evaluate the impact of strategies addressing adult mental health status and care during the pandemic and to guide interventions for disproportionately affected groups."

## Disparities and Health Equity

### ***News in Brief***

Long read: "Medicine for the people: As more and more doctors awaken to the political determinants of health, the U.S. medical profession needs a deeper vision for the ethical meanings of care" ([Boston Review](#)).

### ***JAMA and Racism***

Long read: "Troubling podcast puts JAMA, the 'voice of medicine,' under fire for its mishandling of race" ([STAT](#)).

Long read: "A top medical journal said 'no physician is racist.' now scientists are boycotting: After a podcast from the prestigious journal JAMA questioned whether systemic racism exists in medicine, doctors and researchers are pressing for sweeping changes" ([BuzzFeed News](#)).

### ***Peer-Reviewed Articles***

JAMA Netw Open: [Association of Human Mobility Restrictions and Race/Ethnicity-Based, Sex-Based, and Income-Based Factors With Inequities in Well-being During the COVID-19 Pandemic in the United States](#) (07 April 2021)

"Question: Were state-specific mobility restrictions during the first wave of the COVID-19 pandemic in the United States associated with the well-being of individuals in groups that have historically been marginalized on the basis of race/ethnicity, sex, or income?

Findings: In this cross-sectional study of 1 088 314 US adults, African American individuals with low income, Hispanic individuals, and women of all racial/ethnic groups had higher risks of experiencing unemployment, class cancellations, food insufficiency, and mental health problems during the first wave of the COVID-19 pandemic.

Meaning: These findings suggest that public health policies that ignore existing distributions of risks to well-being may be intrinsically regressive if they fail to target necessary relief measures to individuals who have historically experienced the most marginalization."

Clin Infect Dis: [Racial and Ethnic Differences and Clinical Outcomes of COVID-19 Patients Presenting to the Emergency Department](#) (02 April 2021)

"Since the introduction of remdesivir and dexamethasone for severe COVID-19 treatment, few large multi-hospital system US studies have described clinical characteristics and outcomes of minority COVID-19 patients who present to the emergency department (ED).

This cohort study from the Cerner Real World Database (87 US health systems) from December 1, 2019 to September 30, 2020 included PCR-confirmed COVID-19 patients who

self-identified as non-Hispanic Black (Black), Hispanic White (Hispanic), or non-Hispanic White (White). The main outcome was hospitalization among ED patients. Secondary outcomes included mechanical ventilation, intensive care unit care, and in-hospital mortality. Descriptive statistics and Poisson regression compared sociodemographics, comorbidities, receipt of remdesivir, receipt of dexamethasone, and outcomes by racial/ethnic groups and geographic region.

94,683 COVID-19 patients presented to the ED. Blacks comprised 26.7% and Hispanics 33.6%. Nearly half (45.1%) of ED patients presented to hospitals in the South. 31.4% (n=29,687) were hospitalized. Lower proportions of Blacks were prescribed dexamethasone (29.4%; n=7,426) compared to Hispanics (40.9%; n=13,021) and Whites (37.5%; n=14,088). Hospitalization risks, compared to Whites, were similar in Blacks (Risk Ratio (RR)=0.94; 95% CI:0.82, 1.08; p=0.4) and Hispanics RR=0.99 (95% CI:0.81, 1.21; p=0.91), but risk of in-hospital mortality was higher in Blacks, RR=1.18 (95% CI:1.06, 1.31; p=0.002) and Hispanics, RR=1.28 (95% CI: 1.13, 1.44; p < 0.001).

Minority patients were overrepresented among COVID-19 ED patients, and while they had similar risks of hospitalization as Whites, in-hospital mortality risk was higher. Interventions targeting upstream social determinants of health are needed to reduce racial/ethnic disparities in COVID-19."

Ann Intern Med: [Spatial Inequities in COVID-19 Testing, Positivity, Confirmed Cases, and Mortality in 3 U.S. Cities : An Ecological Study](#) (30 March 2021)

"Background: Preliminary evidence has shown inequities in coronavirus disease 2019 (COVID-19)–related cases and deaths in the United States.

Objective: To explore the emergence of spatial inequities in COVID-19 testing, positivity, confirmed cases, and mortality in New York, Philadelphia, and Chicago during the first 6 months of the pandemic.

Design: Ecological, observational study at the ZIP code tabulation area (ZCTA) level from March to September 2020.

Setting: Chicago, New York, and Philadelphia.

Participants: All populated ZCTAs in the 3 cities.

Measurements: Outcomes were ZCTA-level COVID-19 testing, positivity, confirmed cases, and mortality cumulatively through the end of September 2020. Predictors were the Centers for Disease Control and Prevention Social Vulnerability Index and its 4 domains, obtained from the 2014–2018 American Community Survey. The spatial autocorrelation of COVID-19 outcomes was examined by using global and local Moran I statistics, and

estimated associations were examined by using spatial conditional autoregressive negative binomial models.

Results: Spatial clusters of high and low positivity, confirmed cases, and mortality were found, co-located with clusters of low and high social vulnerability in the 3 cities. Evidence was also found for spatial inequities in testing, positivity, confirmed cases, and mortality. Specifically, neighborhoods with higher social vulnerability had lower testing rates and higher positivity ratios, confirmed case rates, and mortality rates.

Limitations: The ZCTAs are imperfect and heterogeneous geographic units of analysis. Surveillance data were used, which may be incomplete.

Conclusion: Spatial inequities exist in COVID-19 testing, positivity, confirmed cases, and mortality in 3 large U.S. cities."

JAMA Intern Med: [Association of Race/Ethnicity With Likeliness of COVID-19 Vaccine Uptake Among Health Workers and the General Population in the San Francisco Bay Area](#) (30 March 2021)

"This cross-sectional survey study investigates COVID-19 vaccine intentions among racially and ethnically diverse samples of health workers and the general population."

## **Risk, Transmission, and Exposure**

### ***News in Brief***

"It's a filtration system, it's a phone, it's a headset, it's a face mask -- and it can be yours for \$299" ([Medpage Today](#); [NYT](#)).

"Why indoor spaces are still prime COVID hotspots: Risks shoot up when virus particles accumulate in buildings, but it's not clear how best to improve ventilation" ([Nature](#)).

## ***Peer-Reviewed Articles***

Emerg Infect Dis: [Epidemiologic Evidence for Airborne Transmission of SARS-CoV-2 during Church Singing, Australia, 2020](#) (05 April 2021)

"An outbreak of severe acute respiratory syndrome coronavirus 2 infection occurred among church attendees after an infectious chorister sang at multiple services. We detected 12 secondary case-patients. Video recordings of the services showed that case-patients were seated in the same section, >15 m from the primary case-patient, without close physical contact, suggesting airborne transmission."

Anaesthesia: [The effect of respiratory activity, non-invasive respiratory support and facemasks on aerosol generation and its relevance to COVID-19](#) (30 March 2021)

"Respirable aerosols (< 5 µm in diameter) present a high risk of SARS-CoV-2 transmission. Guidelines recommend using aerosol precautions during aerosol-generating procedures, and droplet (> 5 µm) precautions at other times. However, emerging evidence indicates respiratory activities may be a more important source of aerosols than clinical procedures such as tracheal intubation. We aimed to measure the size, total number and volume of all human aerosols exhaled during respiratory activities and therapies. We used a novel chamber with an optical particle counter sampling at 100 l.min<sup>-1</sup> to count and size-fractionate close to all exhaled particles (0.5–25 µm). We compared emissions from ten healthy subjects during six respiratory activities (quiet breathing; talking; shouting; forced expiratory manoeuvres; exercise; and coughing) with three respiratory therapies (high-flow nasal oxygen and single or dual circuit non-invasive positive pressure ventilation). Activities were repeated while wearing facemasks. When compared with quiet breathing, exertional respiratory activities increased particle counts 34.6-fold during talking and 370.8-fold during coughing ( $p < 0.001$ ). High-flow nasal oxygen 60 at l.min<sup>-1</sup> increased particle counts 2.3-fold ( $p = 0.031$ ) during quiet breathing. Single and dual circuit non-invasive respiratory therapy at 25/10 cm.H<sub>2</sub>O with quiet breathing increased counts by 2.6-fold and 7.8-fold, respectively (both  $p < 0.001$ ). During exertional activities, respiratory therapies and facemasks reduced emissions compared with activities alone. Respiratory activities (including exertional breathing and coughing) which mimic respiratory patterns during illness generate substantially more aerosols than non-invasive respiratory therapies, which conversely can reduce total emissions. We argue the risk of aerosol exposure is underappreciated and warrants widespread, targeted interventions."

Clin Infect Dis: [Assessing asymptomatic, pre-symptomatic and symptomatic transmission risk of SARS-CoV-2](#) (27 March 2021)

"The relative contributions of asymptomatic, pre-symptomatic and symptomatic transmission of SARS-CoV-2 have not been clearly measured although control measures may differ in response to the risk of spread posed by different types of cases.

We collected detailed information on transmission events and symptom status based on laboratory-confirmed patient data and contact tracing data from four provinces and one municipality in China. We estimated the variation in risk of transmission over time, and the severity of secondary infections, by symptomatic status of the infector.

There were 393 symptomatic index cases with 3136 close contacts and 185 asymptomatic index cases with 1078 close contacts included into the study. The secondary attack rate among close contacts of symptomatic and asymptomatic index cases were 4.1% (128/3136) and 1.1% (12/1078), respectively, corresponding to a higher transmission risk from

symptomatic cases than from asymptomatic cases (OR: 3.79, 95% CI: 2.06, 6.95). Approximately 25% (32/128) and 50% (6/12) of the infected close contacts were asymptomatic from symptomatic and asymptomatic index cases, respectively, while more than one third (38%) of the infections in the close contacts of symptomatic cases were attributable to exposure to the index cases before symptom onset. Infected contacts of asymptomatic index cases were more likely to be asymptomatic and less likely to be severe.

Asymptomatic and pre-symptomatic transmission play an important role in spreading infection, although asymptomatic cases pose a lower risk of transmission than symptomatic cases. Early case detection and effective test-and-trace measures are important to reduce transmission."

Clin Infect Dis: [Associations between measures of social distancing and SARS-CoV-2 seropositivity: a nationwide population-based study in the Netherlands](#) (27 March 2021)

"This large nationwide population-based seroepidemiological study provides evidence on the effectiveness of physical distancing (>1.5m) and indoor group size reductions on SARS-CoV-2 infection. Additionally, young adults may play an important role in viral spread, opposed to children up until 12 years of age with whom close contact is permitted."

Nat Med: [SARS-CoV-2 infection of the oral cavity and saliva](#) (25 March 2021)

"Despite signs of infection—including taste loss, dry mouth and mucosal lesions such as ulcerations, enanthema and macules—the involvement of the oral cavity in coronavirus disease 2019 (COVID-19) is poorly understood. To address this, we generated and analyzed two single-cell RNA sequencing datasets of the human minor salivary glands and gingiva (9 samples, 13,824 cells), identifying 50 cell clusters. Using integrated cell normalization and annotation, we classified 34 unique cell subpopulations between glands and gingiva. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) viral entry factors such as ACE2 and TMPRSS members were broadly enriched in epithelial cells of the glands and oral mucosae. Using orthogonal RNA and protein expression assessments, we confirmed SARS-CoV-2 infection in the glands and mucosae. Saliva from SARS-CoV-2-infected individuals harbored epithelial cells exhibiting ACE2 and TMPRSS expression and sustained SARS-CoV-2 infection. Acellular and cellular salivary fractions from asymptomatic individuals were found to transmit SARS-CoV-2 ex vivo. Matched nasopharyngeal and saliva samples displayed distinct viral shedding dynamics, and salivary viral burden correlated with COVID-19 symptoms, including taste loss. Upon recovery, this asymptomatic cohort exhibited sustained salivary IgG antibodies against SARS-CoV-2. Collectively, these data show that the oral cavity is an important site for SARS-CoV-2 infection and implicate saliva as a potential route of SARS-CoV-2 transmission."

Gut: [COVID-19 transmission following outpatient endoscopy during pandemic acceleration phase involving SARS-CoV-2 VOC 202012/01 variant in UK](#) (24 March 2021)

"Infection prevention and control (IPC) measures put in place during the first phases of the COVID-19 pandemic were effective in reducing endoscopy-related transmission while allowing recovery of activity.

In late 2020 a novel, more infectious, SARS-CoV-2 variant (VOC 202012/01) was associated with a second 'surge' or acceleration phase in the UK. We sought to measure whether pre-existing IPC guidance would be sufficient to prevent transmission in this scenario.

Prospective data were collected from eight UK centres for n=2440 procedures. Pre-endoscopy, nine (0.37%) asymptomatic patients were positive for SARS-CoV-2 by nasopharyngeal swab (NPS) testing and their procedures deferred. Post endoscopy, 30 (1.27%) developed symptoms suspicious for COVID-19, with 15 (0.65%) testing positive on NPS. Three (0.12%) cases were attributed to potential transmission from endoscopy attendance. All 15 patients recovered fully requiring only community treatment.

Although we report cases potentially transmitted by endoscopy attendance in this latest study, the risk of COVID-19 transmission following outpatient endoscopy remains very low. Thus, IPC measures developed in earlier pandemic phases appear robust, but our data emphasise the need for vigilance and strict adherence to these measures in order to optimally protect both patients and staff."

PLoS One: [SARS-CoV-2 is associated with high viral loads in asymptomatic and recently symptomatic healthcare workers](#) (18 March 2021)

"Healthcare workers (HCW) are at increased risk of SARS-CoV-2 infection from both patients and other HCW with coronavirus disease 2019 (COVID-19). RT-PCR cycle threshold (Ct) values of SARS-CoV-2  $\leq 34$  and the first 7–9 days of symptoms are associated with enhanced infectivity. We determined Ct values and duration of symptoms of HCW with a positive SARS-CoV-2 test. As HCW often assume their greatest risk of acquiring SARS-CoV-2 is working on a COVID-19 unit, we also determined Ct values and symptom duration of inpatients with a positive SARS-CoV-2 test.

From 6/24/2020-8/23/2020, Ct values and duration of symptoms from 13 HCW, 12 outpatients, and 28 inpatients who had a positive nasopharyngeal swab for SARS-CoV-2 were analyzed.

Among HCW with a positive SARS-CoV-2 test, 46.2% (6/13) were asymptomatic and requested testing due to an exposure to someone with COVID-19; 83.3% (5/6) of those exposures occurred in the community rather than in the hospital. The median Ct value of HCW was 23.2, and 84.6% (11/13) had a Ct value  $\leq 34$ . The median Ct value of 29.0 among outpatients with COVID-19 did not significantly differ from HCW. In contrast, inpatients with a positive SARS-CoV-2 test had a median Ct value of 34.0 ( $p = 0.003$ ), which translated into a median ~1,000-fold lower viral load than observed in HCW. Among those with symptoms

related to COVID-19, no (0/6) HCW compared to 50% (6/12) of inpatients had symptoms for at least one week ( $p = 0.04$ ).

At our institution, asymptomatic COVID-19 accounted for nearly half of the cases among HCW. Symptomatic HCW had high viral loads and short duration of symptoms, both of which are associated with peak infectivity. Infection prevention programs should educate HCW on these findings in an effort to increase adherence to the requirement to maintain six feet separation in workspaces and breakrooms, in addition to consistently wearing personal protection equipment."

## **Impact on Healthcare Workers**

### ***News in Brief***

"Young doctors faced down the pandemic but aren't sure about their futures" ([BuzzFeed News](#)).

Long read: "Pandemic burnout is rampant in academia: Remote working, research delays and childcare obligations are taking their toll on scientists, causing stress and anxiety" ([Nature](#)).

### ***Peer-Reviewed Articles***

JAMA: [Symptoms and Functional Impairment Assessed 8 Months After Mild COVID-19 Among Health Care Workers](#) (07 April 2021)

"This cohort study describes COVID-19-related symptoms persisting 8 months after SARS-CoV-2 infection among Swedish health care workers and self-reported effects of the residual symptoms on respondents' home, work, and social function."

JAMA Netw Open: [Experiences of a Health System's Faculty, Staff, and Trainees' Career Development, Work Culture, and Childcare Needs During the COVID-19 Pandemic](#) (01 April 2021)

"Question: What are the associations of the COVID-19 pandemic with career development and what are the work culture and childcare needs of employees and trainees?

Findings: In this survey study, most participants with children did not have childcare fully available and many considered leaving the workforce and were worried about their career. Being female with children or having a clinical job role was associated with consideration for leaving the workforce and reducing hours.

Meaning: These findings suggest that a substantial number of employees and trainees experienced major stress and work disruptions because of the COVID-19 pandemic."

## Reinfections, Coinfection, and Other Infectious Diseases

### News in Brief

"Covid-19 reinfections are rare — but without better data, we don't know how rare" ([STAT](#)).

The dramatic shift to test for COVID has led to 'mass disruptions' to test, screen, surveil, and treat sexually transmitted infections ([AP](#)).

"A research team based in the Democratic Republic of the Congo (DRC) has documented an instance of Ebola relapse in a patient—which sparked a 91-case transmission chain—who had been vaccinated prior to the first infection" ([CIDRAP](#); see also: [NEJM report](#)).

Are you a bird watcher? Look, don't touch, and wash your hands after restocking your bird feeder—you don't want *Salmonella* from those pretty songbirds ([CDC](#)).

Finally, a quick heads up for folks in the mid-Atlantic region about an outbreak of a different kind: the cicadas are coming ([Vox](#); check out the map!).

## Statistics

### Global

09 APR 2021: 134,102,467 confirmed cases and 2,905,149 deaths in 192 countries/regions

02 APR 2021: 129,761,773 confirmed cases and 2,830,059 deaths in 192 countries/regions

26 MAR 2021: 125,629,394 confirmed cases and 2,757,473 deaths in 192 countries/regions

### United States

#### top 5 states by cases

	TOTAL US	CA	TX	FL	NY	IL
Cases	31,003,585	3,690,031	2,819,729	2,104,686	1,933,807	1,269,078
Deaths	560,127	60,129	49,017	33,906	50,898	23,740

[JHU CSSE](#) as of 1000 EDT 09 April 2021

Virginia	Total (state)	Chesapeake	Hampton	Newport News	Norfolk	Portsmouth	Suffolk	Virginia Beach
Cases	632,625	19,856	9,784	13,086	16,598	8,519	7,546	33,866
Hospitalizations	27,099	929	339	380	920	631	425	1,478
Deaths	10,451	278	162	215	239	180	180	368

[VA DOH](#) as of 1000 EDT 09 April 2021